



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|-----------------------------------|------------------------|
| 10/520,239 | 07/18/2005 | Peter John Sadler | 14084-005US1 / RJW/CP6263 | 5058 |
| 23575 7590 06/18/2009 CURATOLO SIDOTI CO., LPA 24500 CENTER RIDGE ROAD, SUITE 280 CLEVELAND, OH 44145 | | | EXAMINER CHANDRAKUMAR, NIZAL S | |
| | | | ART UNIT 1625 | PAPER NUMBER |
| | | | MAIL DATE 06/18/2009 | DELIVERY MODE PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--|--------------------------------------|--|
| Office Action Summary | Application No. 10/520,239 | Applicant(s) SADLER ET AL. | |
| | Examiner NIZAL S. CHANDRAKUMAR | Art Unit 1625 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 May 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26-34 and 36-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26-34 and 36-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants response filed 10/520239 is acknowledged.

Response to Remarks:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the previous office action, it was stated that

The description of the instant formulae is replete with technical incongruity to such an extent that a meaningful assessment of the protection sought for, is impossible.

Amendments to claims deleting "a" from the description of the Y-L-Y' is insufficient to overcome the previously presented rejections. Applicants arguments are limited to "a". Office action 07/10/2007 recommends explicit structural delineation (see page 9, second paragraph, last sentence).

Some examples of technical issues with the instant description are shown below:

Applicant's amendments to claim overcomes part of the rejection. The instant amendments define Y-L-Y' as two possibilities II and III. Because of the definition of Y-L-Y' as bidentate negatively charged, instant amendment limits the L part of Y-L-Y' to sp² carbon linked to 2c. The definition for L in the last four lines of these claims is not

Art Unit: 1625

in agreement with the claimed possibilities for 2c because none of the defined possibilities for 2c is divalent. Also see rejection under 35 U.S.C. 112 first paragraph with regards to dimeric Example-7 of the instant specification.

The reason for the renaming of R2c of base claim 26 in dependent claim 32 as R is not clear as the definitions for these variables seem to be the same. Appropriate explanation is requested as this could necessitate 112-2 rejection of claim 32 for lacking antecedent basis.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following statement preceded the previously presented rejection:

The following rejection is based on claim interpretation limited by the vague and indefinite nature of the instant claims. See rejection under 35 U.S.C. 112, second paragraph

Previously presented rejection of independent claims 26 and 36 under 112-first paragraph with regards to lacking enabling disclosure for making and using the compounds is maintained for reasons of record.

The amendments to claims as suggested by the examiner is insufficient to overcome the rejection because of the vagueness of the claims. There is one dimeric complex based on Y-L-Y' formula III (Example 7 of the specification page 24), but this

Art Unit: 1625

compound does not have any disclosed biological properties. Also see rejection under 112-2 second paragraph with regards to dimeric complexes. As such enabling disclosure with regards (use aspect of the requirement) to dependent claims containing subject matter pertaining to Y-L-Y' as formula (III) is not present. While such compounds are makeable (see Example 7, page 24), there is nothing in the disclosure that would indicate such compounds would satisfy the 'use' aspect of the enablement requirement. See pages 9-10 of the previously presented office action. Also note that these claims encompass compounds that contain the elements of the variable L. As previously indicated there is no enabling disclosure in the specification for compounds containing any elements of the variable L (see rejection under 112 second paragraph).

The specification is enabling for subject matter pertaining to Y-L-Y' as formula (II) as found in claim 36 as this claim is limited to ovarian adenocarcinoma unlike the claim 26 which uses the umbrella term that includes any and all cancers. This acknowledgment is consistent with the rejection under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previously presented rejections based on the teachings of Kuhlwein et al. Kramer et al. and Everacere et. al. are withdrawn in view of the amendment to claims.

The rejection of claims 26-30, 32-34, 36-40, 42-44 under 35 U.S.C. 102(b) as being anticipated by Carmona et al. (J.Chem Soc. Dalton Trans. 1990, 1463-1476) is maintained for reasons of record.

Applicant's arguments are based on MPEP 2131 with regard to preamble element 'method of treating'. Applicants state that the determination of whether a preamble limits a claim is made on a case-by-case basis in light of the facts in the case; there is no litmus test defining when a preamble limits the scope of a claim. Thus, applicant argue, the instant claim limitations relating to "method of treating" cancer is not taught by Carmona and thus can not be ignored. However this is not found persuasive as the structural limitation are able to stand alone, further because the preamble element in this case is inherent to the Ru compounds. The process of use of Ru compounds in cancer therapy is not an unobvious use as such this is not an issue of new use for old compound.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject

Art Unit: 1625

matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Previously presented rejection of claims 26-30, 32-34, 36-40, 42-44 rejected under 35 U.S.C. 103(a) as being unpatentable over Morris et al. WO 2001030790 in view of Kuhlwein et al. (Z. anorg. allg. Chem. 623 (1997) 1211-1219), and Carmona et al. (J.Chem Soc. Dalton Trans. 1990, 1463-1476) is maintained.

Applicant's arguments are fully considered, in conjunction with the amendments to the claims, but are not persuasive.

Applicant's arguments are based mainly on the following:

1. Considerable difference between instant compounds and prior art compounds.
2. The rejection is based on 'Obvious to try' rationale and the office action failed to apply TSM standard to allege obviousness.

Response:

1. The formula (I) still encompasses compounds of Carmona et. al. The methods disclosed in the instant case for making the claimed compounds, including the fluoborate salts are identical to the methods taught by Carmona et. al. (see instant specification Example 6 in page 23). The compounds of Kuhlwein et al. differ from the instant formula compounds in the variables R1c, R2c and R3c. However these groups are commonly used substituents in medicinal chemistry. In combination, compounds of

Art Unit: 1625

these two citations are not 'considerably' different from the compounds of the instant case because, both teach bidentate Y-L-Y' beta-keto carbonyl anions compounds. In agreement with applicants arguments it is/was originally acknowledged that the Morris et al reference does not teach the instantly claimed compounds as the ligands on the Ru are different, but the reference is used here to support of the medicinal properties of Ru complexes in chemotherapy.

2. Previous office action took into consideration, teachings, suggestion and motivation in the prior art cited in addition to the disclosure as a whole in light of the general knowledge of one skilled in the art of cancer chemotherapy at the time of the instant specification. The knowledge that Ru compounds can be used in cancer therapy is well known at the time of the instant application. The established utility of Pt compounds in treating cancer and the elementary observation that Ru belongs to Group VIII transition metals were known at the time of the instant application provide for motivational elements to explore Ru compounds. See Sava, Chapter 4, Metal compounds in Cancer Therapy, Published **1994**. The introduction to this article is shown below:

Art Unit: 1625

The examination of the biological roles of ruthenium complexes as well as the possibility of producing ruthenium-based drugs, active in the treatment of human malignancies, is believed to have begun with the discovery of the antineoplastic activity of cis-dichlorodiammine platinum(II) (hereafter called cisplatin). The fate of ruthenium compounds is common to that of many other transition metals. Based on the elementary observation that ruthenium belongs to the Group VIII transition metals (the so-called platinum group), ruthenium compounds have been studied in comparison to cisplatin in order to ameliorate cisplatin toxicity and potency. In other words, like palladium, rhodium, iridium, osmium and other transition metals, ruthenium was studied in order to obtain compounds which are more potent than cisplatin and under the same conditions in which cisplatin is active. Therefore, from most investigations it is expected that ruthenium compounds will reduce tumour growth by a mechanism of interaction with cell DNA, similar to that shown by cisplatin.

Because of the above teaching, the success with cisplatin (Pt compound) would suggest to one of skill in the art, to test the Ru compounds of Carmona et al. that were available at the time of the instant application. The prior art compounds fall within the scope of the instantly claimed formula and structurally analogous to cisplatin; one skilled in the art would be motivated to make minor modifications, changing one member of the platinum group metal to another. Obviousness based on similarity of structure and functions entails motivation to make the claimed compound in expectation that compounds of similar in structure will have similar properties; therefore, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new compounds.

The specification does not disclose any unexpected results for secondary consideration.

The rejection of claims 31 and 41 under 35 U.S.C. 103(a) is withdrawn; These claims are limited to dimeric compounds; No such compounds are disclosed in the cited article. These claims are, however rejected under 35 U.S.C. 112 for not satisfying the use aspect of the enablement requirement. As such including these claims in obviousness rejection would be inconsistent.

Note: Kramer et al. and Everacere et. al references are not used here in view of amendments to claims. The basis of the obviousness is not dependent on these references.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Art Unit: 1625

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nizal S Chandrakumar/
Examiner, Art Unit 1625

/D. Margaret Seaman/

Primary Examiner, Art Unit 1625